Levalbuterol Compared to Racemic Albuterol*

Efficacy and Outcomes in Patients Hospitalized With COPD or Asthma

Terrance Truitt, MD, FCCP; James Witko, MD, FCCP; and Michael Halpern, MD, PhD

Study objectives: **To compare clinical efficacy, patient outcomes, and medical costs in hospitalized patients treated with levalbuterol to those treated with racemic albuterol.**
Design: **Retrospective chart review.**
Setting: **A 180-bed community hospital.**
Patients: **Patients admitted to Halifax Regional Hospital with a diagnosis code for COPD or asthma from July 1 to December 31, 1998, and from July 1 to December 31, 1999, were eligible. In 1998, 125 patients were treated with nebulized racemic albuterol (2.5 mg q4h). In 1999, 109 patients were treated with levalbuterol (1.25 mg q8h).**
Measurements and results: **Clinical efficacy was evaluated by the number of nebulizer treatments, improvement in symptoms and objective clinical findings, the length of hospital stay, and hospital discharge disposition. Medication and total hospital costs were calculated based on *Red Book* listings and Medicare reimbursement rates. Levalbuterol-treated patients required significantly fewer treatments with β-agonists (mean [± SD] number of treatments, 19.0 ± 12.7 vs 30.8 ± 24.0; $p < 0.001$) and ipratropium bromide (mean number of treatments, 9.4 ± 11.5 vs 23.2 ± 25.1; $p < 0.001$) than did racemic albuterol-treated patients. The mean length of hospital stay in the levalbuterol group was almost 1 day less than that in the racemic albuterol group (4.7 ± 2.9 vs 5.6 ± 4.2 days, respectively; $p < 0.058$). Significantly more patients were readmitted to the hospital within 30 days in the racemic albuterol group compared with the levalbuterol group (16.4% vs 5.7%, respectively; $p = 0.01$). The mean total cost of nebulizer therapy was significantly greater for patients receiving racemic albuterol than for those receiving for levalbuterol ($112 ± 101 vs $61 ± 43, respectively; $p < 0.001$). The mean total hospital costs per patient were less for levalbuterol compared with racemic albuterol ($2756 ± 2079 vs $3225 ± 2714, respectively; $p = 0.11$). Regression analysis controlling for diagnosis, baseline FEV_1, and ipratropium use indicated that levalbuterol was associated with a length-of-stay savings of 0.91 days ($p = 0.015$), a total cost savings of $556 ($p = 0.013$), and a decrease in the likelihood of hospital readmission of 67% ($p = 0.056$).**
Conclusion: **Compared with patients treated with racemic albuterol, those treated with levalbuterol required less medication, had shorter lengths of hospital stay, had decreased costs for nebulizer therapy and hospitalization, and appeared to have a more prolonged therapeutic benefit. These findings support using levalbuterol as first-line therapy for hospitalized adults with COPD or asthma.** ***(CHEST 2003; 123:128–135)***

Key words: asthma; COPD; efficacy; levalbuterol; nebulizer; pharmacoeconomics; racemic albuterol; respiratory therapy

Since its approval in 1982, the β_2-agonist racemic albuterol has been a mainstay in treating the bronchial smooth muscle spasm associated with reversible obstructive airway diseases such as COPD and asthma.[1] With regular use, a progressive decline in the bronchoprotective efficacy of racemic albuterol, leading to a decreased interval between doses and diminished bronchodilation, has been observed.[2,3] Up to 8% of patients who receive racemic

*From the Halifax Regional Hospital (Drs. Truitt and Witko), South Boston, VA; and Exponent, Inc (Dr. Halpern), Alexandria, VA.
The abstraction of the data contained in medical charts and data analysis were funded by Sepracor, Inc.
Received November 14, 2001; revision accepted August 13, 2002.

Correspondence to: Michael Halpern, MD, PhD, Exponent, Inc, 1800 Diagonal Rd, Suite 355, Alexandria, VA 22314; e-mail: mhalpern@exponent.com

albuterol via nebulization actually develop paradoxical bronchospasm, a life-threatening condition.[4,5]

One reason for this decline in efficacy could be related to the composition of racemic albuterol. With one exception (levalbuterol), all marketed forms of β-agonists are racemic mixtures that are composed of a 50:50 ratio of (R)-isomers and (S)-isomers. (R)-albuterol (hereafter referred to as levalbuterol) is the therapeutically active bronchodilator. Current evidence indicates that (S)-albuterol is devoid of any bronchodilatory activity.[6] Rather, (S)-albuterol increases intracellular calcium in airway smooth muscle cells *in vitro*, which promotes smooth muscle contraction and opposes bronchodilation.[7,8] This also results in the increased bronchial reactivity of human airway smooth muscle *in vitro*.[9] In guinea pigs, (S)-albuterol enhances airway hyperresponsiveness to nonspecific spasmogens.[9–12] (S)-albuterol also may recruit eosinophils to the airway and may promote their activation.[13,14] Clinically, (S)-albuterol promoted greater hypersensitivity and increased methacholine-induced bronchospasm in patients with moderately severe asthma.[6]

In contrast, levalbuterol is the active component of racemic albuterol that, when administered as the single isomer, avoids all of the potentially detrimental effects of (S)-albuterol. In asthmatic patients, treatment with levalbuterol decreased hypersensitivity to methacholine to a greater degree and with a longer duration of action than does treatment with racemic albuterol.[6,15] In outpatient studies,[16–18] asthma patients who were treated with levalbuterol experienced a significantly greater increase in FEV_1, a longer duration of action, and fewer side effects. In the emergency department, levalbuterol improved pulmonary function significantly more than racemic albuterol[19] and significantly decreased the number of hospitalizations compared to racemic albuterol.[20] These data suggest that the (S)-albuterol within racemic albuterol limits the beneficial pharmacologic activity of levalbuterol.

To date, the efficacy of levalbuterol has been confirmed in several well-controlled outpatient clinical trials[16–18] in adults, adolescents, and children aged 4 to 11 years. The purpose of the present investigation was to evaluate the impact of levalbuterol on clinical effectiveness, patient outcomes, and direct medical costs through a retrospective chart review of hospitalized adult patients in a "real-world" community-based setting.

Materials and Methods

A retrospective chart review was conducted of patients who had been admitted to Halifax Regional Hospital, Halifax County, VA. Charts were reviewed from two seasonally matched periods. During the first 6-month period (July 1 to December 31, 1998), patients were treated with racemic albuterol, with a target care path of 2.5 mg given every 4 h and as medically necessary. During the second 6-month period (July 1 to December 31, 1999), patients were treated with levalbuterol, with a target care path of 1.25 mg given every 8 h and as medically necessary. These care paths were the standard of care in the institution at the time. Additional care path standards that were in place during both periods included the parenteral administration of steroids for all COPD and asthma patients, as well as the administration of antibiotics for all COPD and asthma patients with a known or suspected infectious component. Patients had an *International Classification of Diseases* hospital admission diagnosis code for asthma (493.xx) or COPD (491.xx, 492.xx, or 496). Patients with concomitant diagnoses of cognitive disturbances or cancer were excluded from the study. To avoid biasing the study results, all patients meeting the entry criteria were included in the study. A sample size calculation or power test was not considered to be necessary for this retrospective chart review.

Institutional review board approval was not obtained for this retrospective chart review, as there was no patient contact and all data viewed by nonhospital personnel were anonymous (patient identifiers were seen only by hospital-employed chart reviewers, and these identifiers were not included in the data abstraction process). A standard data collection form was designed, and information was extracted from the chart by medical personnel at Halifax Hospital. The chart audit included demographic characteristics, hospital admission diagnosis, preexisting comorbidities, length of stay in each hospital ward (*ie*, ICU vs general ward), dates and types of respiratory services rendered, prescribed respiratory therapy regimen focusing on nebulized bronchodilator use (*ie*, racemic albuterol, levalbuterol, or ipratropium bromide), pulmonary function tests at hospital admission and discharge, and patient disposition on hospital discharge. Information on other factors related to the patients' conditions, such as time since diagnosis, was not abstracted from the medical charts.

The primary clinical end point was the total number of nebulizer treatments required. Secondary end points included changes in pulmonary function test results (*ie*, FEV_1), duration of hospitalization, disposition following hospitalization, and pharmacy and resource utilization costs. Resource utilization end points included the costs of respiratory therapy, the use of in-hospital respiratory prescription drugs, and the length of hospitalization. The number of nebulizer treatments was used as a proxy for the number of respiratory therapist procedures. The drug costs used were the average wholesale prices listed in the 1999 *Red Book*. Hospital stay costs were estimated using the maximum reimbursable Medicare rates for a particular ward type (ICU vs general ward). This value is a *per diem* cost, representing the total average services received by a patient during a day of hospitalization (such as respiratory therapy services) but not including medications. Thus, respiratory medication costs were determined, but the cost of respiratory therapy itself was not separable from the *per diem* hospital cost. Medicare payments, in addition to having the advantage of being standard national values for comparing the costs of care between different institutions, are conservative and generally are accepted as proxies for the actual cost of a service.

Statistical analyses were performed to compare study variables between the levalbuterol and racemic albuterol groups overall, as well as separately for the asthma and COPD treatment subgroups, with statistical significance based on an α value of 0.05 (two-tailed test) using the Student *t* test to compare group means. All p values ≤ 0.1 are presented. Those p values that are > 0.1 are indicated as "not significant." Data that were not normally distributed were analyzed using the Mann-Whitney test for nonparametric independent samples. The Cochran-Mantel-Haenszel χ^2 test was used for categoric data as appropriate.

Regression analysis was conducted *post hoc* to determine the role of diagnosis, baseline FEV_1, and ipratropium bromide use on length of stay, cost, and hospital readmissions. For regression analyses of length of stay and cost, log transformations of the dependent variables were used in multivariate linear regressions to correct for the nonnormal distribution of the dependent variables. Logistic regression was used to evaluate the impact of levalbuterol on hospital readmissions within 30 days of hospital discharge (dichotomous dependent variable, readmitted yes/no) while controlling for diagnosis, baseline FEV_1, and ipratropium bromide use.

Results

Charts from 231 patients who met the study criteria were identified and reviewed. One hundred twenty-five patients (COPD, 90 patients; asthma, 35 patients) were admitted to the hospital during the first period and were treated with racemic albuterol. One hundred six patients (COPD, 87 patients; asthma, 19 patients) were admitted to the hospital during the second period and were treated with levalbuterol. The demographics of patients treated with either racemic albuterol or levalbuterol were not significantly different (Table 1). Compared to asthma patients, COPD patients tended to be older (38 vs 65 years of age), were more often men (27% vs 46%), and were more often white. Approximately 95% of patients received therapy with steroids during the hospitalization. Of the patients receiving steroids, 96% were administered parenterally. There were no differences in steroid use between the study periods (data not shown). Hospital admission and discharge values for FEV_1 and FVC were not significantly different between the two groups for each diagnosis studied. Overall, patients in both treatment groups demonstrated comparable improvement in FEV_1 and FVC from hospital admission to discharge (Table 2).

Table 1—*Demographics*

Variables	Racemic Albuterol	Levalbuterol
Patients, No.	125	106
Mean age,* yr	57.1 (21.5)	58.2 (16.1)
Men, %	43.2	40.6
White, %	71.2	67.9
Patients hospitalized in the past year, %	55.2	47.6
Hospitalizations per patient within the past year,* No.	0.80 (1.0)	0.80 (1.1)
Patients with discharge diagnosis of asthma, %	28.0	17.9
Patients with discharge diagnosis of COPD, %	72.0	82.1

*Values given as mean (SD), with no significant differences among baseline parameters.

Table 2—*Pulmonary Function

Variables	Racemic Albuterol	Levalbuterol
Asthma patients, No.	35	19
Admission FEV_1		
L	1.28 (0.55)	1.42 (0.68)
% predicted	44.6 (16.5)	48.6 (21.8)
Discharge FEV_1		
L	1.75 (0.71)	1.85 (0.60)
% predicted	57.0 (19.0)	63.6 (18.6)
Admission FVC, L	1.89 (0.80)	2.14 (0.81)
Discharge FVC, L	2.38 (0.84)	2.49 (0.73)
COPD patients, no.	90	87
Admission FEV_1		
L	0.95 (0.55)	0.87 (0.42)
% predicted	36.2 (19.3)	32.9 (14.7)
Discharge FEV_1		
L	1.03 (0.56)	0.99 (0.48)
% predicted	36.7 (19.8)	37.1 (16.4)
Admission FVC, L	1.57 (0.64)	1.48 (0.62)
Discharge FVC, L	1.75 (0.70)	1.68 (0.66)

*Values given as mean (SD), with no significant differences among treatment groups.

Patients in the levalbuterol treatment group required significantly fewer nebulizer treatments than did those in the racemic albuterol treatment group (mean [± SD] mean number of treatments, 19.0 ± 12.7 vs 30.8 ± 24.0, respectively; $p < 0.001$) [Fig 1, *top*, *A*]. Patients treated with levalbuterol required an average of 38% fewer nebulizer treatments per hospital stay. The difference between treatment groups was even more noticeable among the asthmatic patients, among whom those in the levalbuterol treatment group needed 53% fewer nebulizer treatments than did those in the racemic albuterol treatment group (mean number of treatments, 30.0 ± 23.6 vs 14.1 ± 9.2 per hospital stay, respectively; $p < 0.002$). Patients treated with levalbuterol also required 29% fewer days of nebulizer therapy than did those treated with racemic albuterol (mean, 5.5 ± 4.3 vs 3.9 ± 2.3 days, respectively; $p < 0.001$) [Fig 1, *bottom*, *B*]. Again, the difference was even greater in the group of asthma patients, in which patients in the levalbuterol treatment group needed 43% fewer days of nebulizer therapy than did those in the racemic albuterol treatment group (4.6 ± 3.7 vs 2.6 ± 1.2 days, respectively; $p < 0.008$). Patients receiving levalbuterol therapy also required significantly less adjuvant respiratory therapy with ipratropium bromide. The racemic albuterol group received more than twice as many days of ipratropium bromide therapy as did the levalbuterol group (mean, 4.2 ± 4.3 vs 2.0 ± 2.6 days, respectively; $p < 0.001$) and needed 60% more ipratropium bromide treatments (mean, 23.2 ± 25.1 vs 9.4 ± 11.5 treatments, respectively; $p < 0.001$). Fewer patients treated with levalbuterol required

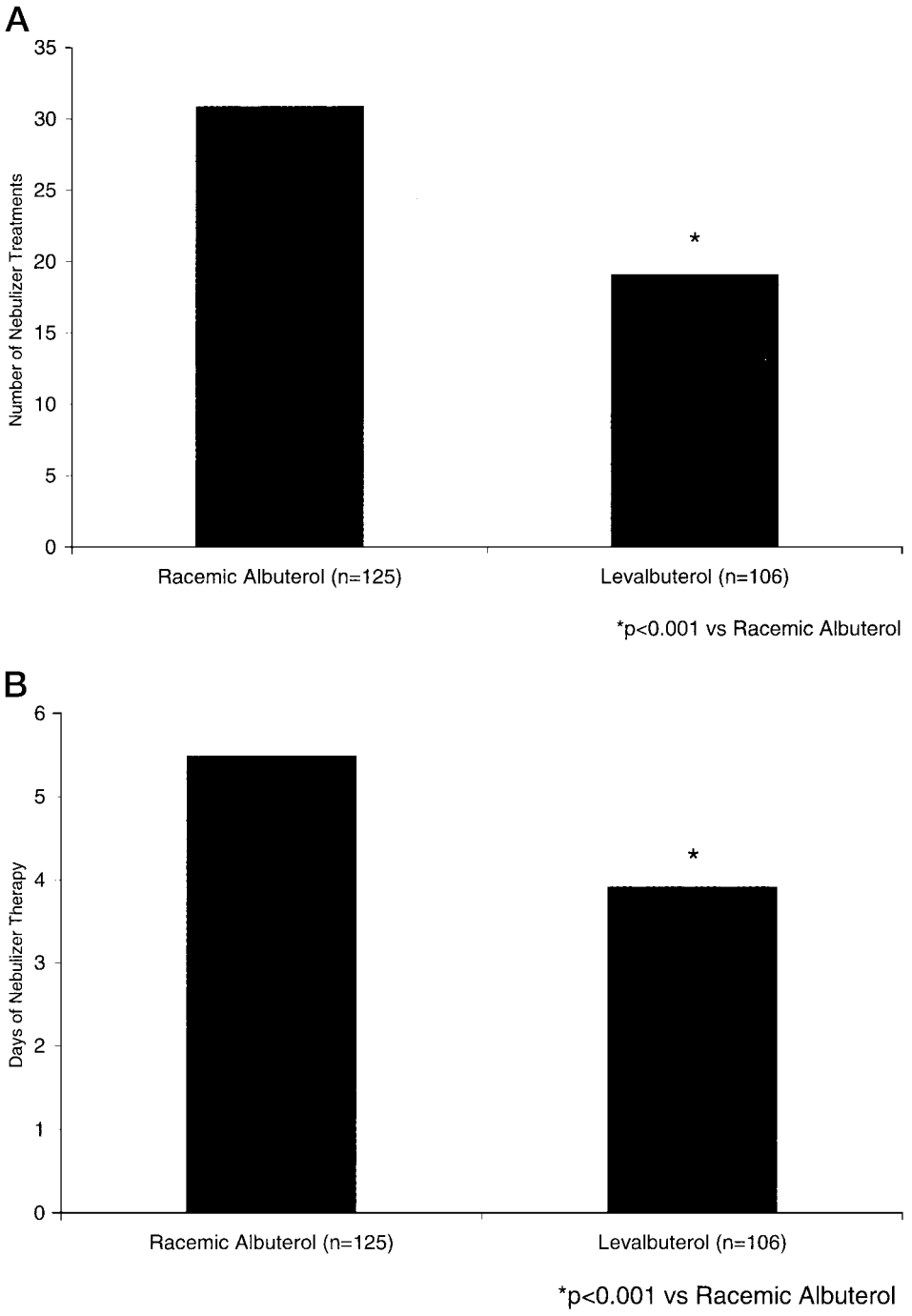

FIGURE 1. *Top, A*: total number of nebulizer treatments per patient. Patients treated with levalbuterol required about 38% fewer scheduled nebulizer treatments than did patients who had been treated with racemic albuterol. * = $p < 0.001$ vs racemic albuterol. *Bottom, B*: total number of days receiving nebulizer therapy per patient. Patients treated with levalbuterol had 29% fewer days receiving nebulizer therapy than did patients who had been treated with racemic albuterol. * = $p < 0.001$ vs racemic albuterol.

rescue nebulizations of any kind for the treatment of acute exacerbations (levalbuterol, 13.6% of patients; racemic albuterol, 16.5% of patients; difference not significant). This trend toward a decreased need for rescue medication was evident throughout the review, with 15.8% of asthmatic patients in the levalbuterol treatment group needing treatments as medically necessary compared to 18.8% of those in the racemic albuterol treatment group (difference not significant), and 13.1% of

COPD patients in the levalbuterol treatment group receiving treatments as medically necessary compared to 15.7% of those in the racemic albuterol treatment group (difference not significant).

These reductions in both β_2-agonist and ipratropium bromide usage resulted in a significantly decreased total cost of nebulizer therapy for levalbuterol patients. As a group, patients treated with levalbuterol incurred nebulization therapy costs that were 45% less than those incurred by the patients treated with racemic albuterol (racemic albuterol patients, \$112 ± 101; levalbuterol patients, \$61 ± 43; $p < 0.001$). The β_2-agonist cost associated with levalbuterol therapy was 28.7% less than that associated with racemic albuterol therapy (\$37 ± 25 vs \$53 ± 41, respectively; $p < 0.001$). Similarly, the cost for ipratropium bromide that was associated with levalbuterol therapy was 59.4% less than that associated with racemic albuterol therapy (\$24 ± 29 vs \$59 ± 64, respectively; $p < 0.001$). A 56% reduction in the total cost of nebulizer therapy was observed in the asthma patients treated with levalbuterol compared to the cohort treated with racemic albuterol (racemic albuterol patients, \$99 ± 94; levalbuterol, \$44 ± 36; $p < 0.005$). For COPD patients, nebulizer therapy costs among those receiving levalbuterol decreased by 44% (racemic albuterol patients, \$116 ± 104; levalbuterol patients, \$65 ± 44; $p < 0.0001$).

Overall, patients treated with levalbuterol had shorter hospital stays than did those treated with racemic albuterol. The mean length of hospital stay for all patients treated with levalbuterol (4.7 ± 2.9 days) was 16% less than that for all patients treated with racemic albuterol (5.6 ± 4.2 days). This difference of 0.9 days approached statistical significance ($p = 0.058$). The asthma patients who had been treated with levalbuterol had a 27% shorter length of hospital stay, and COPD patients had a 16% shorter hospital stay compared to patients with the same diagnoses who had been treated with racemic albuterol, although this difference was not statistically different (Table 3).

The total hospital costs for patients treated with levalbuterol were less than those for patients treated with racemic albuterol (difference not significant; Fig 2). The hospital costs were composed of costs for dormitories, personnel, and other resource utilization but excluded medication. The mean costs incurred by asthmatic patients who had been treated with racemic albuterol were \$2,503 ± 1,994, while those incurred by patients who had been treated with levalbuterol were \$1,856 ± 931 (26% less). For COPD patients, the mean hospital cost for those treated with racemic albuterol was \$3,506 ± 2,908, while for those treated with levalbuterol the incurred mean costs \$2,952 ± 2,209 (16% less). On average, for both asthma and COPD patients, levalbuterol therapy reduced the cost of hospital care, by about \$650 and \$550 per patient, respectively ($p = 0.1$ for asthma patients; difference not significant for COPD patients).

Table 3—*Disposition of Hospitalized Patients

Variables	Racemic Albuterol	Levalbuterol	p Value
Asthma patients			
Length of hospitalization, d	4.5 (3.6)	3.3 (1.6)	0.097
Discharge to home	100	94.7	NS
Readmission within 30 d	0	5.3	NS
COPD patients			
Length of hospitalization, d	6.1 (4.4)	5.1 (3.0)	0.07
Discharge to home	90.0	96.6	0.08
Readmission within 30 d	23	5.8	0.0012

*Values given as mean (SD) or percent, unless otherwise indicated. NS = not significant.

Patient disposition was somewhat different according to β_2-agonist therapy and admitting diagnosis (Table 3). Approximately ≥ 95% of asthma patients were discharged to home. Of the COPD patients, 96.6% of those treated with levalbuterol were discharged to home, as were 90% of those treated with racemic albuterol ($p = 0.08$). In the group of COPD patients who had been treated with racemic albuterol, 2.2% were discharged to subacute care facilities and 6.7% were discharged to long-term care facilities (data not shown). No patients in the levalbuterol group required subacute care, and 2.3% were discharged to long-term care facilities (data not shown). These differences were not statistically significant.

Overall, the rate of hospital readmission within 30 days following hospital discharge differed between patients treated with racemic albuterol and those treated with levalbuterol (Table 3). Almost threefold more patients who had been treated with racemic albuterol were readmitted to the hospital than were patients who had been treated with levalbuterol (16.4% and 5.7%, respectively; $p = 0.01$). In the racemic albuterol treatment group, 23% of the COPD patients required hospital readmission compared with 5.8% of the COPD patients in the levalbuterol treatment group ($p = 0.0012$). Differences in hospital readmission rates among asthma patients were not statistically significant. Among all study patients who had been readmitted within 30 days of hospital discharge, 67% had primary diagnoses of respiratory conditions.

Regression analysis was conducted to determine the potential confounding effect of baseline FEV_1, the use of ipratropium bromide, and diagnosis on length of stay, cost, and hospital readmissions. The results from the regression analyses are presented in

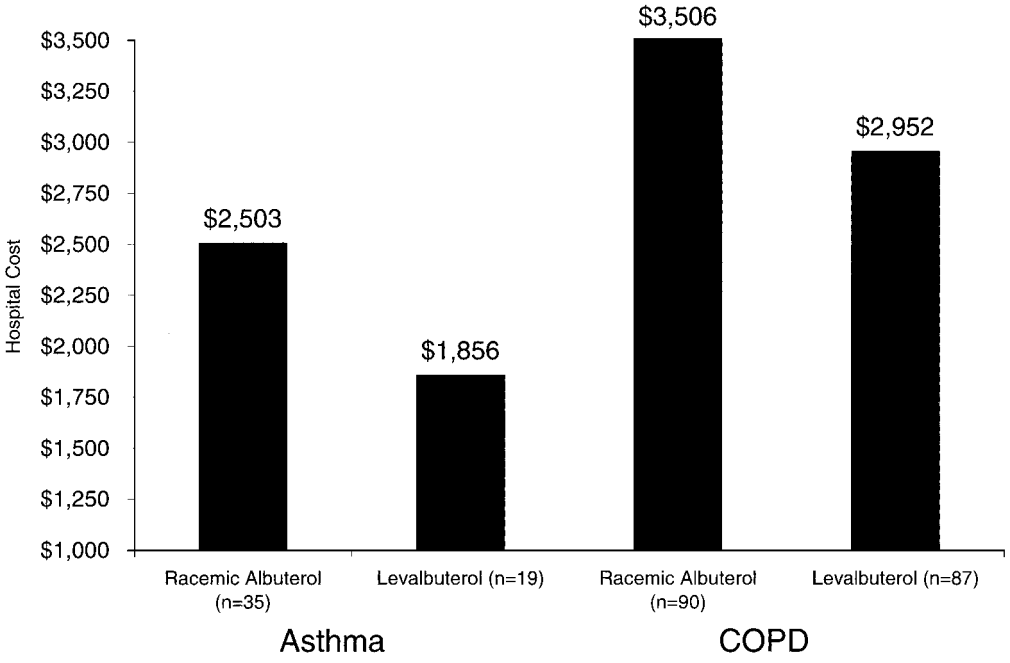

FIGURE 2. Hospital costs. Costs include dormitory, staff, and medical service costs but exclude pharmacy costs. Asthma patients who had been treated with levalbuterol incurred costs of care that were $647 less than those for patients who had been treated with racemic albuterol. COPD patients who had been treated with levalbuterol incurred $553 less in costs than did patients who had been treated with racemic albuterol. These differences were not significantly different.

Table 4. When controlling for these factors, levalbuterol treatment was associated with a 0.91-day savings in length of stay ($p = 0.015$), a $556 savings in total cost ($p = 0.013$), and a 67% decrease in the likelihood of hospital readmission within 30 days of discharge (odds ratio, 0.33; 95% confidence limits, 0.11, 1.03; $p = 0.06$).

DISCUSSION

In this retrospective chart audit at Halifax Hospital, levalbuterol afforded clinical and pharmacoeconomic advantages over racemic albuterol for the treatment of bronchospasm in adult patients with COPD or asthma. Levalbuterol significantly reduced the amount of nebulizer therapy and its associated costs, as well as the length of hospital stay, both of which contributed to a reduction in total hospital costs. Because there were no other changes at Halifax Hospital in hospital policy or in the standard treatment paradigm for asthma and COPD patients between the two time periods of this study (including changes in the use of steroids, antibiotics, or other medications), and because the

Table 4—*Regression Analysis Results*

	Length of Hospitalization*			Total Cost†			Readmission Within 30 Days‡		
Independent Variables	Parameter Estimate	SE	p Value	Parameter Estimate	SE	p Value	Parameter Estimate	SE	p Value
Use of levalbuterol§	− 0.20842	0.08292	0.0128	− 0.22401	0.09093	0.0147	− 1.1014	0.5756	0.0557
Asthma diagnosis	− 0.17304	0.10141	0.0896	− 0.14153	0.11120	0.2047	− 1.7223	1.0616	0.1047
Received atrovent treatment	0.07022	0.09233	0.4479	0.04822	0.10124	0.6344	0.0320	0.6325	0.9597
Admission FEV_1	− 0.25041	0.07901	0.0018	− 0.21213	0.08664	0.0153	− 0.2761	0.5224	0.5972
Model intercept	1.81605	0.12852	< 0.0001	8.13997	0.14092	< 0.0001	− 1.3204	0.8198	0.1073

*Adjusted $R^2 = 0.1074$ (goodness of fit).
†Adjusted $R^2 = 0.0683$ (goodness of fit).
‡Hosmer-Leweshow statistic = 10.0421 (goodness of fit; $p = 0.2621$).
§Xopenex; Sepracot Inc; Marlborough, MA.

attending pulmonologists were the same during the two study periods, it is likely that these observed outcomes are attributable to the use of levalbuterol in place of racemic albuterol.

There are a number of limitations associated with this study. All data were obtained from medical charts. As such, the types of information that were available were limited, and it was not possible to validate the available information using other sources. Furthermore, all data were from a single institution, which may limit the generalizability of the results. Data that may have influenced the likelihood of hospital readmission, such as the duration of disease and the role of social workers or case managers, were not collected, although the case managers and their procedures were the same for entire study period. An additional limitation is the lack of masking in the study design. However, this design is more relevant to understanding the "real-world" impacts of a new therapy. Because levalbuterol was the standard of care during the second period of the study in 1999, no biases were introduced from the introduction of an "experimental" therapy or from expectations by patients when participating in a prospective research study. Thus, we believe that the open-label presentation of levalbuterol did not introduce biases into the study and is likely to provide results that are more applicable to actual patient care.

Studies[19,21] comparing the clinical effectiveness of levalbuterol to that of racemic albuterol in the emergency department have shown that levalbuterol is more effective in improving pulmonary function than is the same amount of isomer administered as racemic albuterol. In children presenting to the emergency department with acute asthma, the improvement in pulmonary function translated into a significant reduction in the number of hospital admissions.[20] In this study, an analysis of the hospital admission and discharge pulmonary function tests demonstrated that, as expected, the administration of both β_2-agonists resulted in equivalent improvements in FEV_1, because patients were treated as necessary to achieve clinical end points that enabled hospital discharge. Reductions in both length of stay and the number of hospital days on which nebulizer therapy with levalbuterol treatment was required suggested that these patients demonstrated clinical improvement earlier (which is expected to correlate to an improvement in FEV_1) than the patients who were treated with racemic albuterol.

The ability to change the target nebulizer dosing schedule to every 8 h with levalbuterol from the standard racemic albuterol schedule of every 4 to 6 h may have contributed to the need for the 38% fewer treatments observed in this study. It has been suggested that fewer doses of levalbuterol (1.25 mg) are needed because levalbuterol produces greater bronchodilation than racemic albuterol for a longer period of time.[16,18] The need for less frequent dosing allows for fewer nebulizer treatments and less nebulizer medication during the course of treatment, as was seen in the current study. The earlier onset and prolonged effect of bronchodilation with levalbuterol also may have resulted in a decreased need for concomitant ipratropium bromide therapy. The absence of (S)-albuterol in the levalbuterol treatments may have contributed in a number of ways to the findings. Eliminating the potential adverse effects of (S)-albuterol, which are known to be both proinflammatory[13,14] and bronchoconstrictive,[9–12] may have contributed to the tendency toward a decreased length of hospital stay and an increased rate of hospital discharge to home. The absence of (S)-albuterol may allow for the persistence of bronchodilation that has been observed with levalbuterol, especially in patients with severe disease. Nelson et al[16] demonstrated that, after 28 days, basal lung function (measured as the non-drug-affected FEV_1) improved with levalbuterol treatment, while it did not change with racemic albuterol. This difference was most pronounced and significant in patients who were receiving no concomitant steroid therapy.[16] Similar improvements may contribute to the overall lower hospital readmission rate with levalbuterol and, in particular, in the COPD patients. The decreased hospital readmission rate may be evidence of the therapeutic activity of levalbuterol, despite the fact that patients were generally discharged from the hospital with orders for receiving racemic albuterol via metered-dose inhaler as rescue therapy (a levalbuterol metered-dose inhaler is currently unavailable). Although information on hospital discharge medications or medication use in the post-hospital discharge period was not collected, the routine hospital discharge practices and treatment patterns did not differ between the two time periods of this study. Further investigation is needed to evaluate the reasons for the difference in hospital readmittance rates between patients receiving the two therapies.

Finally, the financial benefits of levalbuterol were made clear in several areas. Fewer nebulizer treatments and less need for concomitant inhaled medication decreased both medication and hospital costs. Presumably, the decreases in hospital costs were derived from both decreased respiratory therapy time and decreased length of stay. The overall decrease in hospital readmissions (which often are not reimbursable) following levalbuterol therapy should contribute to cost savings. These additional cost savings were not included in our calculations. Even after controlling for diagnosis, baseline FEV_1, and ipratropium use, levalbuterol was associated with a 0.91-day savings in

hospital length of stay ($p = 0.015$), a $556 savings in total cost ($p = 0.013$), and a 67% decrease in the likelihood of hospital readmission ($p = 0.056$). In a randomized, double-blind, emergency department study[20] in 482 children, 46% of patients treated with 2.5 mg racemic albuterol were admitted to the hospital, compared with 35% of patients who received 1.25 mg levalbuterol ($p < 0.02$). Thus, levalbuterol has been shown to afford clinical and outcome benefits in the hospital preadmission phase by significantly reducing the number of patients who were admitted to the hospital. The present investigation has extended these findings and demonstrated an additional benefit for the inpatient phase of hospital care.

In summary, rapid-onset β_2-agonist agents such as racemic albuterol have been mainstays of therapy for reactive airway diseases. The recent successful isolation of the active (R)-isomer levalbuterol provides a new option for the treatment of COPD and asthma. This retrospective chart audit demonstrated that good clinical performance and significant economic advantages are associated with levalbuterol therapy compared with racemic albuterol therapy. These findings support using levalbuterol as first-line therapy for hospitalized adults with COPD or asthma.

ACKNOWLEDGMENT: The authors thank Julie Bellet, MD, Kendyl Schaefer, MSc, and Franklin Cerasoli, Jr, PhD, for their contribution to the development of this manuscript.

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